

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
11 December 2003 (11.12.2003)

PCT

(10) International Publication Number
WO 2003/102222 A3

(51) International Patent Classification⁷: C12Q 1/00, 1/48,
G01N 33/68, 35/08

(21) International Application Number:
PCT/NL2003/000408

(22) International Filing Date: 30 May 2003 (30.05.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
02077146.5 31 May 2002 (31.05.2002) EP

(71) Applicant (for all designated States except US): KIADIS
B.V. [NL/NL]; Niels Bohrweg 11-13, NL-2333 CA Leiden
(NL).

(72) Inventors; and

(75) Inventors/Applicants (for US only): IRTH, Hubertus
[DE/NL]; Rooseveltlaan 112 2HG, NL-1078 NP Amster-
dam (NL). LETZEL, Thomas [DE/DE]; Kernnatenstrasse
35, 80639 Munich (DE).

(74) Agent: PRINS, A.W.; Nieuwe Parklaan 97, NL-2587 BN
Den Haag (NL).

(81) Designated States (national): AE, AG, AL, AM, AT (util-
ity model), AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,

CH, CN, CO, CR, CU, CZ (utility model), CZ, DE (util-
ity model), DE, DK (utility model), DK, DM, DZ, EC, EE
(utility model), EE, ES, FI (utility model), FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN,
MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU,
SC, SD, SE, SG, SK (utility model), SK, SL, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

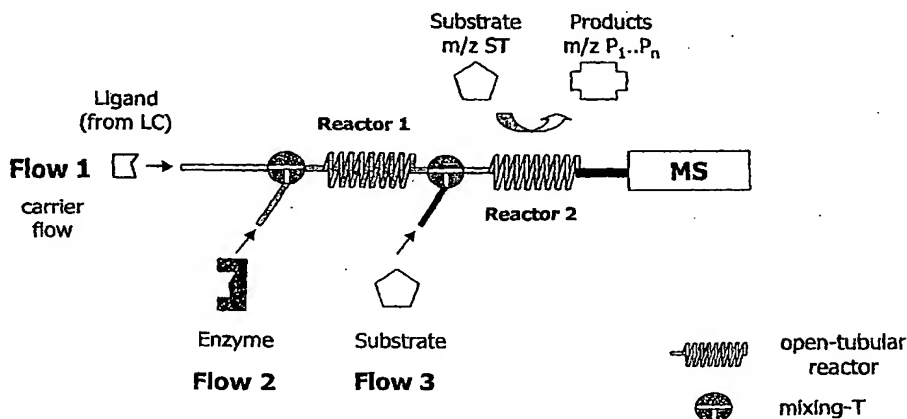
— with international search report
— before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the international search report:
12 February 2004

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: CONTINUOUS-FLOW ENZYME ASSAY WITH MASS SPECTROMETRY DETECTION

On-line enzyme MS assay – System 1



(57) **Abstract:** The present invention relates to an on-line detection method comprising the steps of: contacting an effluent of a fractionation step with a controlled amount of an enzyme; allowing the enzyme to interact with analytes suspected to be present in the effluent; addition of a controlled amount of a substrate for said enzyme; allowing a reaction of the enzyme with the substrate providing one or more modified substrate products; and detection of unreacted substrate, or a modified substrate product using a mass spectrometer.